

Applicant: Michael J. Heller et al.

U.S. Serial No.: 09/358,788

Filed: July 22, 1999

Page 3 of 11: Amendment In Response To October 18, 2011 Final Office
Action As A Submission Accompanying A Request For Continued
Examination Under 37 C.F.R. §1.114

Amendments to the Claims

This listing of claims will replace all prior versions, and
listings of claims in the application:

Listing of Claims:

Claims 1-48 (Canceled).

49. (Currently Amended) A method for analyzing a sample
oligonucleotide sequence in solution comprising:

- (a) forming a plurality of individually electronically addressable microscopic locations on a substrate, each microscopic location comprising a micro-electrode;
- (b) providing a permeation layer adjacent to said micro-electrode in each of said microscopic locations, said permeation layer having selective diffusion properties thereby permitting the free transport of counter-ions to said micro-electrode and inhibiting large binding entities from physical contact with said micro-electrode;
- (c) providing an attachment layer adjacent to said permeation layer in each of said microscopic locations;
- (d) electronically immobilizing one or more anchor sequences to said attachment layer in individually selected microscopic locations, wherein said one or more anchor sequences comprise oligonucleotide sequences capable of hybridizing with said sample oligonucleotide sequence;
- (e) ~~subjecting said individually selected microscopic locations to an electric field prior to hybridization~~
~~and~~ contacting said sample oligonucleotide sequence with said one or more anchor sequences thereby allowing said

Applicant: Michael J. Heller et al.

U.S. Serial No.: 09/358,788

Filed: July 22, 1999

Page 4 of 11: Amendment In Response To October 18, 2011 Final Office
Action As A Submission Accompanying A Request For Continued
Examination Under 37 C.F.R. §1.114

sample oligonucleotide sequence to hybridize to said one
or more anchor;

(f) subjecting said individually selected microlocations to
an a continuous and constant electric field which moves
unhybridized and partially hybridized sample
oligonucleotide sequences away from said one or more
anchor;

(g) determining whether said sample oligonucleotide sequence
is hybridized to said one or more anchor sequences; and

controlling a level of stringency of hybridization, by
adjusting a power level of said electric field and/or a length
of time said individually selected microlocations are subjected
to said electric field in step (f), to improve said analyzing
of the sample oligonucleotide sequence, by enabling ensuring
removal of partially hybridized sequences and improving the
resolution of single mis-match hybridizations.

Claims 50-56 (Canceled).

57. (Currently Amended) The method of claim 49, wherein ~~said~~
~~subjecting said individually selected microscopic locations to an~~
~~electric field in step (e)~~ additionally comprises subjecting said
individually selected microlocations to an electric field which
concentrates said sample oligonucleotide sequence near said one or
more anchor sequences.

58. (Previously Presented) The method of claim 49, wherein each one
of said one or more anchor sequences is from 6 to 100 bases.

Claims 59-78 (Canceled).

79. (Previously Presented) The method of claim 49, wherein said
sample oligonucleotide sequence is free to move and be transported
between said microscopic locations on said substrate.

Applicant: Michael J. Heller et al.
U.S. Serial No.: 09/358,788
Filed: July 22, 1999
Page 5 of 11: Amendment In Response To October 18, 2011 Final Office
Action As A Submission Accompanying A Request For Continued
Examination Under 37 C.F.R. §1.114

80. (Previously Presented) The method of claim 49, wherein step (g) further comprises:

- (i) adding a probe comprising an oligonucleotide sequence capable of hybridizing to a target oligonucleotide sequence forming part of said sample oligonucleotide sequence that is not hybridized to said one or more anchor sequences, thereby allowing said probe to hybridize to said target oligonucleotide sequence;
- (ii) subjecting said individually selected microscopic locations to an electric field which moves unhybridized probe oligonucleotide sequences away from said one or more anchor sequences; and
- (iii) determining whether said probe is hybridized to said target oligonucleotide sequence.

81. (Previously Presented) The method of claim 49, wherein said permeation layer, said attachment layer, or both, are made from aminopropyltriethoxy silane.

82. (Currently Amended) A method for analyzing a sample oligonucleotide sequence in solution comprising:

- (a) forming a plurality of individually electronically addressable microscopic locations on a substrate, each microscopic location comprising a micro-electrode, and said sample oligonucleotide sequence is free to move and be transported between said microscopic locations on said substrate;
- (b) providing a permeation layer adjacent to said micro-electrode in each of said microscopic locations, said permeation layer having selective diffusion properties thereby permitting the free transport of counter-ions to said micro-electrode and inhibiting large binding

Applicant: Michael J. Heller et al.

U.S. Serial No.: 09/358,788

Filed: July 22, 1999

Page 6 of 11: Amendment In Response To October 18, 2011 Final Office
Action As A Submission Accompanying A Request For Continued
Examination Under 37 C.F.R. §1.114

entities from physical contact with said micro-
electrode;

- (c) providing an attachment layer adjacent to said permeation layer in each of said microscopic locations;
- (d) electronically immobilizing one or more anchor sequences to said attachment layer in individually selected microscopic locations, wherein said one or more anchor sequences comprise oligonucleotide sequences capable of hybridizing with said sample oligonucleotide sequence;
- (e) contacting said sample oligonucleotide sequence with said one or more anchor sequences thereby allowing said sample oligonucleotide sequence to hybridize to said one or more anchor;
- (f) subjecting said individually selected microlocations to ~~an~~ a continuous and constant electric field which moves unhybridized and partially hybridized sample oligonucleotide sequences away from said one or more anchor;
- (g) determining whether said sample oligonucleotide sequence is hybridized to said one or more anchor sequences; and

controlling a level of stringency of hybridization, by adjusting a power level of said electric field and/or a length of time said individually selected microlocations are subjected to said electric field in step (f), to improve said analyzing of the sample oligonucleotide sequence, by enabling ensuring removal of partially hybridized sequences and improving the resolution of single mis-match hybridizations.